Amendments to the Specification

Please amend Paragraphs **[0023]**, **[0031]**, **[0033]**, **[0039]** and **[0045]**, as designated in the application as filed, or Paragraphs **[0027]**, **[0035]**, **[0037]**, **[0046]** and **[0054]**, as designated in the application as published (Publication No. US 2004/0115711 A1), as follows:

[0023] Techniques for fabrication of microscale or nanoscale cantilevers 110, 210, 310, 400, 510 or cantilever arrays 500 are known. (E.g., Baller et al., *Ultramicroscopy*. 82:1-9, 2000; Lang et al., *Appl. Phys. Lett.* 72:383, 1998; Lang et al., *Analytica Chimica Acta* 393:59, 1999; Hansen et al., *Anal. Chem.* 73:1567-71, 2001; Wu et al., *Proc. Natl. Acad. Sci. USA* 98:1560-64, 2001; Fritz et al., 2000; Ilic et al., Appl. Phys. Lett. 77:450-452, 2000; U.S. Patent Nos. 6,074,484; 6,079,255; *see also* <u>*the world wide web at:*</u> [[http://]]monet.physik.unibas.ch/nose/inficon/; [[http://www.]]phantomsnet.com/phantom/net/phantomsconf/doc/Abadal.pdf; [[http://]]lmn.web.psi.ch/annrep/mntech3.pdf; [[http://www.]]nnf.cornell.edu/200lcnfra/200138.pdf; [[http://www.]]princeton.edu/~cml/html/research/biosensor.html). Any such known fabrication method may be used in the practice of the claimed subject matter. Cantilevers 110, 210, 310, 400, 510 known in the field of atomic force microscopy are typically about 100 to 500 micrometers (μm) long and about 1 μm thick. Silicon dioxide cantilevers 110, 210, 310, 400, 510, 600, 700 varying from 15 to 500 μm in length, 5 to 50 μm in width and 320 nanometers (nm) in thickness, that were capable of detecting binding of single *E. coli* cells, have been manufactured by known methods (Ilic et al., *Appl. Phys. Lett.* 77:450, 2000). The material is not limiting, and any other material known for cantilever 110, 210, 310, 400, 510, 600, 700 construction, such as silicon or silicon nitride may be used. In other embodiments of the invention, cantilevers 110, 210, 310, 400, 510 of about 50 μm length, 10 μm width and 100 nm thickness may be used. In certain embodiments of the invention, nanoscale cantilevers 110, 210, 310, 400, 510 as small as 100 nm in length may be used. In some embodiments, cantilevers 110,

210, 310, 400, 510 of between about 10 to 500 μm in length, 1 to 100 μm in width and 100 nm to 1 μm in thickness may be used.

[0031] In one example when analyte molecules bind to the binding surface 630, 730 the cantilever will bend towards the back of the binding surface 690, 790 due to surface tension stress. The bending can be detected by monitoring light reflection from the cantilever 670, 680, 770, 780. The bending force can be counter-balanced by heating the cantilever through the electrical heater 610, 710. The temperature of the cantilever may be measured by monitoring the resistance change of the heater. Temperature of the cantilever may be regulated by controlling the current 650, 750 that passes through or voltage that is applied to the heater. There may be a feedback loop between the optical detector and the heater controller. The optical-electrical control system may be made by standard electrical engineering methods. In one example, the heater 610, 710 and binding area 630, 730 may not overlap so that a temperature change will not affect analyte binding to the cantilever 600, 700. Bending force created by the heater 610, 710 may be calibrated with the optical detector.

[0033] In one exemplary method the cantilever 600, 700 may be functionalized by treating the silicon side of the cantilever with, for example oxygen plasma, to create a thin silicon oxide layer. After this treatment, the cantilever 600, 700 may be functionalized using silanizing reagent following standard procedure known in the art (see also the world wide web at: [[http://]]cgr.harvard.edu/macbeath/research/sm_microarrays/sm_microarrays.html). The linker group to be used for probe (antibody or receptor) attachment may for example include amine, aldehyde, carboxyl, thiol, or hydroxyl group(s).

[0039] In other embodiments of the invention, cantilever 110, 210, 310, 400, 510, 600, 700 deflection may be detected using an optical detection unit. An optical detection unit may comprise a light source, e.g. a laser diode 170, 270, 365, 540 or an array of vertical cavity

surface emitting lasers 170, 270, 365, 540 (VCSEL), and one or more position sensitive photodetectors ~~170, 270, 365, 540~~ 180, 280, 370, 550. A preamplifier may be used to convert the photocurrents into voltages. The light emitted by the light source 170, 270, 365, 540 is directed onto a surface of the cantilever 110, 210, 310, 400, 510, 600, 700 and reflected to one or more photodiodes ~~170, 270, 365, 540~~ 180, 280, 370, 550. In certain embodiments of the invention, a portion of the cantilever 110, 210, 310, 400, 510, 600, 700 may be coated with a highly reflective surface, such as silver, to increase the intensity of the reflected beam. Deflection of the cantilever 110, 210, 310, 400, 510, 600, 700 leads to a change in the position of the reflected light beams. This change can be detected by the position sensitive photodetector 180, 280, 370, 550 and analyzed to determine the deflection of the cantilever 110, 210, 310, 400, 510, 600, 700. The displacement of the cantilever 110, 210, 310, 400, 510, 600, 700 in turn may be used to determine the amount of counterbalancing force required to restore the cantilever 110, 210, 310, 400, 510, 600, 700 to its initial position.

[0045] The manufacturing method is not limiting and any methods known in the art may be used, such as laser ablation, injection molding, molecular beam epitaxy, dip-pen nanolithograpy, reactive-ion beam etching, chemically assisted ion beam etching, microwave assisted plasma etching, focused ion beam milling, electro-oxidation, scanning probe methods, chemical etching, electron beam or focused ion beam technology or imprinting techniques (*e.g.*, U.S. Patent No. 6,146,227; see also the world wide web at: [[http://www.]]mdatechnology.net/techsearch.asp?articleid=510; Bloch *et al.*, "Optics with an atom laser beam," *Phys. Rev. Lett.* 87:123-321, 2001; Ivanisevic *et al.*, "'Dip-Pen Nanolithography on Semiconductor Surfaces," *J. Am. Chem. Soc.*, 123:7887-7889, 2001; Siegel, "Ion Beam Lithography," VLSI Electronics, Microstructure Science, Vol. 16, Einspruch and Watts eds., Academic Press, New York, 1987). Methods for manufacture of nanoelectromechanical systems may be used for certain embodiments of the invention (*e.g.*, Craighead, Science 290:1532-36, 2000). Various forms of microfabricated chips are commercially available from, *e.g.*, Caliper Technologies Inc.

(Mountain View, CA) and ACLARA BioSciences Inc. (Mountain View, CA). Any type of known material may be used for construction of MEMS devices, including but not limited to glass, plastic, ceramic, silicon, silicon oxide, silicon dioxide, silicon nitride, germanium, gallinium arsenide, and metal-based compositions such as metals and/or metal oxides.